Original Article

CEREBROSPINAL FLUID ANALYSIS ACUTE BACTERIAL VERSUS VIRAL MENINGITIS

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ABSTRACT

Objective: To evaluate the cerebrospinal fluid changes in acute bacterial and viral meningitis and the role of the CSF differential in discriminating bacterial and viral meningitis in adult patients.

Methodology: It is an observational study, conducted at the infectious diseases Unit, Rashid hospital Dubai (JCI accredited), United Arab Emirates, from Jan 2005 to Dec 2007. The admitted patients who fulfilled the criteria were included in the study. CT scan brain was done for almost all the patients before the lumber puncture. The CSF analysis was done on the first spinal tap and it included lactate, protein, glucose, cell count, Gram's stain and culture. Other laboratory investigations including liver function test (LFTs), full blood count (FBC), blood sugar, blood culture, coagulation profile and urea electrolytes were also done for all the patients.

Results: A total of 134(86 bacterial and 48 viral) patients fulfilled the inclusion criteria. Among the bacterial meningitis, 74.42% patients were found to be CSF Gram's stain and/or culture positive for bacteria, whereas 25.58% were culture negative. Overall, blood culture was positive in nineteen (29.68%) and negative in forty five (70.31%) patients. In comparison to the viral, the CSF lactate, protein, cell count with predominant polymorphs as well as blood sugar and peripheral white cell count was significantly higher in the bacterial meningitis, *p* value <0.0001. The mean CSF lactate level in bacterial meningitis cases amounted to 14.96 ± 6.13mmol/L with high sensitivity (98.3%) and positive predictive value (73.4%), where as it was significantly lower in the viral group 2.38±0.59mmol/L. However, the CSF glucose was found to be very low in bacterial than viral meningitis, mean 26.50±21.56 vs 67.00±18.96mg/dl (*p* value <0.0001). The hospital stay was longer and mortality rate was also higher in bacterial than viral group, *p* value <0.0001.

Conclusions: CSF analysis is an important diagnostic tool to differentiate acute bacterial from viral meningitis. Furthermore, when Gram stain and culture are negative, the CSF lactate can provide pertinent, rapid and reliable diagnostic information in distinguishing bacterial from viral meningitis.

KEY WORDS: Meningitis, Bacterial, Viral, CSF analysis.

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INTRODUCTION

Accurate initial diagnosis is the corner stone for therapeutic decision making of acute meningitis. Bacterial meningitis is still a very common and serious disease. Death is not uncommon and many who survive are left

permanently disabled. The Cerebrospinal fluid (CSF) analysis, Gram's stain and culture still remains the most useful method of diagnosis of meningitis, but the patients in whom the CSF Gram stain and culture results are negative, there is no test that is definitive for or against the diagnosis of bacterial meningitis. Recently, in many studies the CSF lactate,[1] CRP,[2] serum procalcitonon[3] and CSF and serum glucose ratio[4] have been found useful in differentiating between bacterial and viral meningitis. A combination of test results, however, may permit an accurate prediction of the likelihood of bacterial versus viral meningitis.

This study was undertaken to evaluate the cerebrospinal fluid changes in acute bacterial and viral meningitis and the role of CSF differential, especially the lactate level in discriminating bacterial and viral meningitis.

METHODOLOGY

This was a hospital based study conducted from Jan 2005 to Dec 2007 in the Infectious Diseases Unit of Rashid Hospital Dubai, UAE. Rashid Hospital is one of the biggest tertiary hospitals of Dubai accredited by the Joint Commission International (JCI). A separate proforma was filled for each case entered into the study. The demographic and data about clinical features and laboratory results of the cases were included in each proforma. CT scan brain was done for almost all the patients before the lumber puncture. The CSF analysis was done on the first spinal tap and it included lactate, protein, glucose, cell count, Gram's stain and culture. CSF lactate level was done by Enzymatic Colorimetric method. Other laboratory investigations including liver function test (LFTs), full blood count (FBC), blood sugar, blood culture, coagulation profile and urea electrolytes were also done for all the patients. The diagnosis of meningitis was based on clinical findings and CSF gram staining, culture and chemical analysis. Meningitis was defined as proven to be bacterial by a positive result on gram staining and/or bacterial culture. Meningitis was probably bacterial if CSF was cloudy, the leukocyte count in CSF was >1500/mm^3 with granulocytes representing >50%, the ratio of glucose in CSF to glucose in blood was <0.4 and the level of CSF protein >200mg/dl.[5]

Inclusion criteria:

1. Patient with clinical diagnosis of meningitis and CSF Gram's staining and/or culture positive for bacteria.
2. Patient with clinical and CSF findings suggestive of meningitis with negative CSF Gram's staining and culture but positive blood culture for bacteria.
3. Clinically suspected and CSF changes suggestive of bacterial meningitis but CSF Gram's staining, culture and blood culture negative and these patients were treated for bacterial meningitis(Culture –ve bacterial meningitis).
4. Patients with clinical diagnosis of viral meningitis. The diagnosis of viral meningitis was established by usual clinical and laboratory criteria, including appropriate history and physical examination, CSF pleocytosis, negative bacterial culture and Gram's stain and CSF protein and glucose concentration. The standard text books describe the typical CSF findings in viral meningitis as a pleocytosis of 20-1000 WBC comprised mainly of lymphocytes in the presence of CSF and blood culture negative for bacteria.[6,7]

Exclusion criteria:

1. Patients who received antibiotics before presenting to the hospital.
2. Patients with Tuberculosis and fungal meningitis.
3. Patients with concomitant illness such as HIV/on immunosuppressive therapy.
4. Conditions which can contribute in elevation of CSF lactate such as recent stroke, brain hypoxia/ anoxia, brain trauma and seizures.

The patients were treated according to the current guidelines for the management of acute bacterial and viral meningitis. Data was analyzed by statistical package SAS Enterprise Guide 4.1. A p value of <0.05 was taken as significant for difference in all statistical analysis.

RESULTS

A total of 134 patients fulfilled the inclusion criteria. The mean age ± SD of the patients under this study was 33.73 ± 11.7 years (16-70) and males outnumbered the females 116(86.56%) vs. eighteen (13.43%). No significant age difference was observed in the two groups of meningitis, mean age 34.97±11.43vs33.27±11.58 years. Majority of the patient were expatriates who visited or lived in the UAE. Among the 134 patients; sixty nine (51.49%) were Indian, seventeen (12.68%) UAE nationals, fifteen (11.19%) Bangladeshi, twelve (8.95%) Pakistani and twenty one (15.67%) other nationals. Fever, headache and altered sensorium were the most common presenting symptoms. Signs of meningeal irritation were present in most of the patients.

Out of the 134 patients, eighty six (64.17%) had bacterial meningitis whereas forty eight (35.82%) had viral meningitis. Among the 86 bacterial meningitis patients, Meningococci was isolated in thirty six (41.86%), Strepo.Pneumoniae in twenty two (25.58%), Staph.Aureus in two (2.32%), Klebsiella Pneumoniae in two (2.32%), Strept.Agalactiae in one (1.16%) and E.Coli in 1(1.16%) patient. In twenty two (25.58%) patients no organism was isolated (culture -ve bacterial meningitis) but CSF changes were suggestive of bacterial meningitis and these patients were treated with antibiotic (Fig-1). Out of the 64 culture positive bacterial meningitis patients, CSF Gram's staining and/or culture was positive in 58(90.62%) and negative in seven (10.92%), however in CSF Gram's stain and culture -ve patients, blood culture was found to be positive. Overall, blood culture was positive in the nineteen (29.68%) and negative in 45(70.31%) patients. There were 48 patients who fulfilled the criteria for viral meningitis.

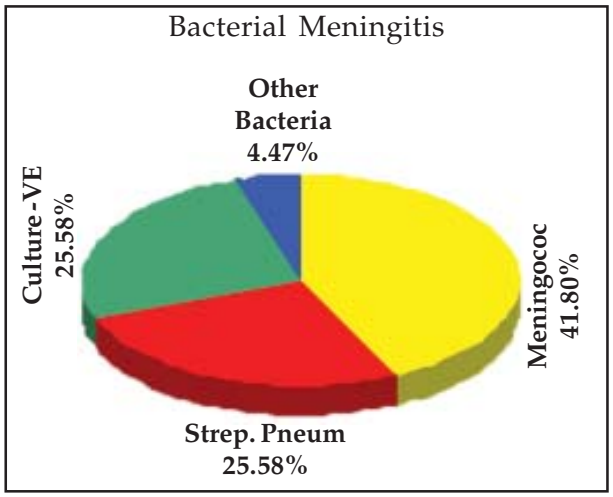

Fig-1: Distribution of the studied group of bacterial meningitis by causative agent, DOHMS, Dubai 2005-2207.

The CSF analysis showed that all patients with bacterial meningitis had lactate level more than(>) 3.8mmol/L except for one patient who had CSF lactate 1.6mmol/L, with high sensitivity(98.3%) and positive predictive value(73.4%) whereas in patients with viral meningitis, none of them had CSF lactate ≥3.8mmol/L. In comparison to viral meningitis, bacterial cases had higher CSF lactate level, with mean lactate level 14.96±6.13mmol/L (range 1.6-35.5) versus 2.38±0.59mmol/L (range 1.6-3.7); with statistically significant difference, *p* value <.0001(Fig-2). The CSF protein level was also high in bacterial than viral meningitis patients, with mean 641.01±428.52 vs. 91.74±44.68mg/dl (*p* value <.0001). The CSF leukocyte count was higher with predominant polymorphs (95%) in bacterial than viral (7%) cases, with mean cell count 4522.25±2809+65 vs. 206.31±218.93cell/mm^3 (*p* value <.0001). In comparison to the viral, the CSF glucose level was found to be lower in

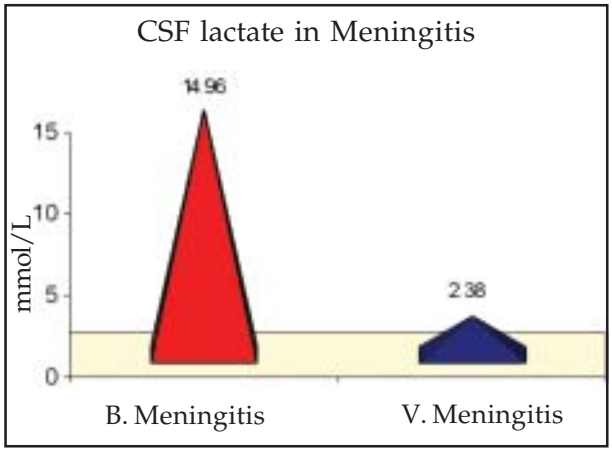

Fig-2: Mean CSF lactate level in acute bacterial and viral meningitis.

bacterial meningitis, mean 26.50±21.56 vs 67.00±18.96mg/dl, with statistically significant difference (*p* value <.0001). In the bacterial group, 50% of the patients had CSF glucose <10mg/dl, whereas none of the patient with viral meningitis had such low CSF glucose level. However, there was no significant difference in CSF changes between Meningococcal and Strep. Pneumoniae meningitis (Table-I).

The blood glucose and peripheral leukocyte count was also high in bacterial than viral meningitis, 179.49±55.10 vs 135.21±39.31mg/dl and 20.76±8.02 vs 8.90+2.25cell/cul respectively (*p* value <.0001). The leucocytosis was present in 91% of the patients in bacterial; where as only 17% of the viral meningitis cases had mild elevation of white cell count. The hospital stay was longer in bacterial than viral meningitis, 9.25±3.40 vs 6.82±2.73 days (*p* value <0.0001). Overall, 16 (11.94%) patients succumbed to death and only one of them had viral meningitis (Table-I).

DISCUSSION

The differential diagnosis between viral and bacterial meningitis is often very difficult.The symptoms and signs of meningitis are often non specific.In one sudy, both Kernings and Brudzinkinski signs had a sensitivity of only 5%, while sensitivity of nucheal rigidity was 30%.[8] Cerebrospinal fluid findings are important in the differential diagnosis of patients with bacterial and viral meningitis.[9] In this study, we noted significant increase in CSF protein level in bacterial meningitis as compared to the viral meningitis, an observation which is also reported by the other investigators.[10] In bacterial meningitis white cell count, usually polymorphs, increases significantly, where as there is mild increase in cell count, mostly lymphocytes in viral meningitis.[11] Results of the study also had the same observation and 95% of the patients with bacterial meningitis had predominant polymorphs, where as only 7% of the patients with viral meningitis had polymorphs pleocytosis. However, Negrini and colleagues had reported that most of the patients with aseptic meningitis had a PMN predominance where neutrophils accounted for >50% of CSF leukocytes.[12] The CSF glucose level usually decreased in bacterial meningitis (<40 percent of simultaneously measured serum glucose) but in viral meningitis CSF glucose is normal or slightly decreased.[9] The findings of the studied case series is consistent with the above observation and >50% of the patients with bacterial meningitis had CSF glucose <10mg/dl, where as none of the patients

Table-I: CSF, Blood glucose and peripheral WBC changes in acute Bacterial and Viral Meningitis.

Etiology	*No.OfPts.*	*Hospit Stay days*	*CSF changes*				*Blood changes*	
			Lactate *(Mean)*	Protein *(Mean)*	Glucose *(Mean)*	Cells *(Mean)*	Glucose *(Mean)*	WBC *(Mean)*
Nisseria meningitides	36	8.69	16.39	806.42	20.15	4947.57	185.96	21.7
Streptococci Pneumoniae	22	11.28	17.22	642.14	17.23	4399.04	187.61	20.9
Other bacteria	6	13.66	12.46	682.33	45.5	3720.8	182.16	12.7
Culture-ve Bacterial Meningitis	22	8.09	10.61	500.61	37.33	3265.47	156.33	20
Viral meningitis	48	6.82	2.38	91.74	67	206.31	135.21	8.9

Ref.range: CSF lactate 1.1-2.4 mmol/L, Proteins 15-45mg/dl, Glucose 40-60% of serum glucose, Cell count ≤5 cell/mm^3, WBC 3.6-11x10^3cells/ul

with viral meningitis had such low CSF glucose level.

Gram's stains of spinal fluid are virtually diagnostic of bacterial meningitis when microorganisms are seen, but negative results of initial Gram's staining do not exclude the diagnosis. The Gram stain is positive in 60% to 90% cases of untreated bacterial meningitis.[4] The likelihood of having a positive Gram stain result also depends on bacterial pathogen causing meningitis: 90% in *Strep.Pneumoniae*, 86% in *H.Influenzae*, 75% in *N.Meningitidis*, 59% in gram negative bacilli and 33% in Listeria monocytogenes the CSF Gram stain is positive.[13] In this study, overall, microorganism was isolated in 74.42% of the patients with bacterial meningitis which is quite similar to the observations reported in the above studies. However, in contrast to the other reports of *Strep.Pneumoniae* being the most common organism in this population,[14] in the studied case series *N.Meningitidis* (41.82%) as the most common organism followed by *Strep.Pneumoniae* (25.58%).

Measurement of CSF lactate has recently been advocated as useful in establishing an early diagnosis of bacterial meningitis, as well as being of some value in separating this entity from aseptic/viral meningitis.[15] In this case series, all patients with untreated bacterial meningitis had elevated level of lactate in CSF except in one. In comparison to viral meningitis, CSF lactate was significantly high in bacterial meningitis (mean 14.96±6.13 vs 2.38±0.59mmol/L), a finding which is consistent with the previous reports.[16] The study done by Gastrin et al have also supported that the CSF lactate is a useful tool in the early diagnosis of bacterial meningitis as well as in differentiating bacterial from viral meningitis.[17] Genton B et al has endorsed the idea that the measurement of the CSF lactate is worth performing when meningitis is suspected, as it appeared to be the best way of distinguishing bacterial from non-bacterial meningitis and it has the highest sensitivity, specificity and predictive value.[18] The CSF lactate was found to be high in both gram-positive and gram negative coccoi and bacilli.[19] Perhaps the most interesting data obtained from this study was the level of CSF lactate which is quite a higher value than reported by the other investigators.[16,20] It was also noticed that the patients who died had higher CSF lactate level (aveg. 19.4mmol/L) than those who were discharged with or without sequellae, an observation which is also reported by the other investigators.[21] However, Robert L, et al in their study suggested that the lactate level in the cerebrospinal fluid did not provide unequivocal evidence of bacterial infection and did not gave assistance to any greater degree than the standard parameters of leukocyte count, protein and glucose contents in the differential diagnosis of bacterial meningitis from that of any other etiology.[22]

CONCLUSION

CSF analysis is an important diagnostic tool to differentiate acute bacterial from viral meningitis. Further more, considering the diagnosting limitation of conventional CSF variables (proteins, glucose and cells) especially when Gram stain and culture are negative, the CSF lactate can provide pertinent, rapid and reliable diagnostic information with higher sensitivity and positive predictive value and is very useful in distinguishing bacterial from viral meningitis.

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